Conservative Therapy for Gastroesophageal Reflux in Infants with Obstructive Pulmonary Disease

Charles W. Callahan DO, MAJ

Gastroesophageal reflux (GER) is a commonly recognized problem in infants. However, it is difficult to demonstrate a causal relationship between GER and recurrent obstructive pulmonary disease (ROPD) in infants. In this review, 3 infants with GER and severe ROPD experienced dramatic improvement with conservative *GER therapy.*

Introduction

All infants have gastroesophageal reflux (GER).[1] Diagnostic tests for GER in infancy are useful to determine whether GER is excessive, prolonged, or is associated with esophageal disease.[2] The evaluation of infants who have GER and symptoms of recurrent obstructive pulmonary disease such as wheezing, cough or noisy breathing may be confusing. To date, there is no single diagnostic test that will prove causation between GER and pulmonary disease.[3-4]

Infants with GER may develop symptoms of airway obstruction by one of two mechanisms: Direct, repeated aspiration of gastric contents[5-6] or reflex stimulation mediated by acidic gastric contents refluxed into the lower esophagus.[7-9] The ideal diagnostic study in a child with recurrent obstructive pulmonary disease and GER would be able to demonstrate a temporal association between GER and increased airway resistance.[3-4] In the absence of the availability of such a study, evidence for GER-causing obstructive pulmonary disease in infants is largely circumstantial.

Three cases of infants with regurgitation and symptoms of severe obstructive pulmonary disease are reviewed, and their symptoms abated after conservative therapy of GER. This suggests that GER may be an etiology of airway obstruction in a subset of otherwise healthy infants and reinforces the potential benefit of conservative GER therapy in these patients.

Chief, Pediatric Pulmonology Clinic
Tripler Army Medical Center
Tripler AMC, HI 96859-5000

Conclusions and opinions expressed are those of the author and do not necessarily reflect the position or policy of the Department of Defense, the Department of the Army the Army Medical Department, or the Health Services Command.

Case 1

BJ is a 6-month old white infant with a 2-month history of congestion and wheezing. Her symptoms developed after an episode of otitis at 4 months of age. She was diagnosed with bronchitis, then hospitalized twice in the next month with asthma and clinical pneumonia. Her wheezing was *continuous* but was especially notable at night. In addition, she had episodes of coughing and hoarseness. She was the term product of an uncomplicated pregnancy. Since her first month of life, she had frequent episodes of regurgitation. She was drinking 36 ounces of cow's-milk formula, 6 ounces every 4 to 6 hours (19.3 cc/kg/feeding, 116 cc/kg/day.) Her medications included cefaclor, theophylline, albuterol syrup, prednisone syrup, erythromycin, as well as albuterol and cromolyn by nebulization. There was no family history of asthma.

On physical examination, BJ was well nourished and developed. Her height (61.2 cm) and weight (9.3 kg) were greater than the 90th percentile for age. Her respiratory rate was 52 breaths per minute. Pulse oximetry on room air was 95%. She had bilateral otitis media. Inspection of the chest revealed mild subcostal retractions and auscultation of her chest, diffuse heterophonous wheezing with coarse inspiratory and expiratory crackles. She had a prominent homophonous (central) wheeze as well. Chest radiograph revealed hyperinflation with marked, diffuse interstitial infiltrates bilaterally. Her sweat chloride level was normal.

Nebulized therapy for reactive airways was continued, with the addition of amoxicillin/clavulanate instead of the cefaclor and erythromycin for the otitis. Conservative therapy for gastroesophageal reflux was instituted including elevation of the head of her crib and the institution of small, more frequent feedings (3 ounces every 3 to 4 hours.) A bedtime fast was also instituted: no feeding within 90 minutes of nap or bedtime. She was to avoid infant seats, car seats, or infant swings for the same period after meals.

She returned 3 days later for a barium swallow. This study demonstrated no GER and normal gastric emptying. Her wheezing had diminished and the coughing had ceased. Five days later when she returned to review the results of the evaluation, she was completely wheeze free, had no subcostal retractions and had a resting respiratory rate of 28 breaths per minute. She continues to grow well and has had no recurrence of symptoms of airway obstruction.

Case 2

SB was a 10-week old girl who had a history of wheezing and cough since 2 weeks of age. She had infrequent episodes of regurgitation, but had spasms of cough and wheezing when

supine and on awakening. At one month of age she was hospitalized with a diagnosis of bronchiolitis. Culture for respiratory syncytial virus was negative. A barium swallow demonstrated no GER and normal gastric emptying. She was discharged on nebulized albuterol and cromolyn, but was hospitalized again 5 days later with the same symptoms. She was discharged on nebulized therapy and erythromycin/sulfamethoxazole. There was a history of asthma in both parents, although there were no smokers at home. She was drinking 6 ounces of Isomil formula 6 times a day (29.6 cc/kg/feeding, 178 cc/kg/day).

On examination, she was well nourished with weight (6.08 kg) greater than the 90th percentile and height (57 cm) at the 50th percentile. Her heart rate was 150 beats per minute and her respiratory rate was 44 while sleeping. Pulse oximetry on room air was 100%. She had an asynchronous respiratory pattern. Auscultation of the chest revealed diffuse heterophonous wheezing and coarse crackles. A chest radiograph revealed hyperinflation and perihilar infiltrates. Her sweat chloride level was normal.

Her nebulized bronchodilators were continued, along with a prednisone burst (1.5 mg/kg/day for 5 days.) She was instructed to follow conservative therapy for GER, including limitation of feedings to 3 ounces every 3 to 4 hours. On phone follow-up 3 days later she had experienced marked improvement. She had no cough or audible wheeze. One month later, she had experienced no recurrence of her symptoms and was growing well.

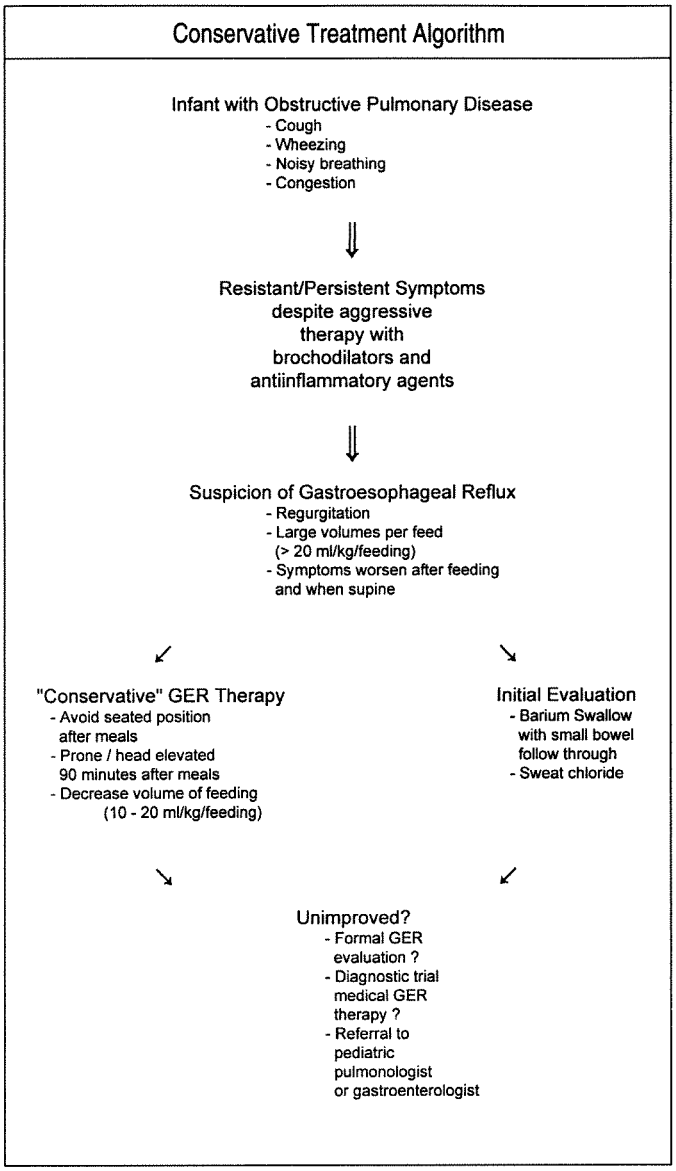
Case 3

CB was a 4-month old with a 3-month history of cough and wheeze. He frequently awakened at night with coughing spells. He had a history of frequent regurgitation. There was no family history of asthma and there were no smokers at home. The infant was drinking 30 to 40 ounces of liquids a day, including 5 seven-ounce bottles of soy formula (26.95 cc/kg/feeding, 158 cc/kg/day formula). He was being treated with albuterol orally and by nebulization. He was well nourished on examination, with height (65.5 cm) greater than the 95th percentile and weight (7.79 kg) greater than the 90th percentile. His heart rate was 120 beats per minute and his respiratory rate was 42 breaths per minute awake. He had subcostal retractions as well as heterophonous and homophonous wheezing and rhonchi on auscultation. Chest radiograph revealed hyperinflation and increased interstitial markings. His sweat chloride level was normal, and a barium swallow showed organoaxial rotation, but normal gastric emptying and no GER.

Therapy with nebulized bronchodilators was continued and a course of amoxicillin/clavulate was begun because of the possibility of a chronic airway infection. He started conservative therapy for GER and his symptoms cleared rapidly with no recurrence of symptoms.

Discussion

The diagnosis of GER in these 3 infants was made qualitatively: All 3 experienced episodes of regurgitation, 2 during their initial office visit. In each case, a barium swallow failed to demonstrate GER despite a strong history of regurgitation, emphasizing the insensitivity of this test in detecting GER.[2] All 3 had symptoms of small airway obstructive pulmonary disease with worsening of symptoms at night. In each case, the symptoms of airway obstruction resolved rapidly after initiation of conservative GER therapy. It could easily be argued that it was the cumulative effect of the bronchodilators or antibiotics that caused the improvement, although the rapidity of resolution suggests otherwise.



When GER occurs in an infant with symptoms of obstructive pulmonary disease, however, it is often impossible to prove that the reflux caused symptoms of airway obstruction.[4] In addition, it is difficult to prove that improvement in pulmonary symptoms is a result of GER therapy. Thus, the decision to treat or to further evaluate the infant with obstructive pulmonary disease and suspected GER is often a clinical one. A trial of conservative therapy for GER at the time a limited evaluation is undertaken often can be helpful.

Conservative therapy of GER usually involves a combination of measures aimed to decrease gastric volume, increase the density of stomach contents, avoid the influence of gravity and increased abdominal pressure on the lower esophageal sphincter. Traditionally, these measures have included: positioning, thickened feeds, small frequent feedings, and bedtime fasting.[3]

In 1947, Neuhauser and Berenberg reported *cardia-esophageal relaxation* in a dozen infants who were diagnosed by barium esophagram.[10] Within 5 years, a case of *cardio-chalasia* and therapy utilizing a *chair* designed by Sister D.N. Roberts

was reported.[11] This patient was considered by the authors, and presumably the editors, to be "sufficiently rare to merit publication of a single case."[11] Success in therapy was attributed to positioning in the chair for all feedings and for an hour afterward. Subsequent papers recommended construction of a similar chair with plaster of paris[12] or plywood.[13]

In the past decade, several studies demonstrated that positioning children with GER prone or prone with head elevated was superior to the infant seat in decreasing the frequency and duration of GER episodes.[14-16] In fact, the chalasia chair might even aggravate the condition it was designed to treat.[15] While car seats, infant swings, and infant seats have not been specifically studied, it is likely that they aggravate the condition as well. In 1990, Orenstein demonstrated in a large prospective study that elevation of the head is no better than flat prone positioning in infants less than 6 months of age.[17] Thus, it is safe to recommend that infants who are suspected of having GER or GER-associated pulmonary disease be positioned prone or possibly prone with their heads elevated after meals. Ideally, they should remain in this position for the time it takes for their stomachs to empty, typically 90 minutes to 2 hours.[18]

For more than 30 years, thickened feedings have been recommended for the treatment of infants with GER, especially those who do not respond to postural therapy.[19] The recommended dose of rice cereal has been one tablespoon or 15 ml of cereal per ounce of formula.[19] Several recent studies have demonstrated that thickening of feeds may actually make GER worse[20-21] and may aggravate pulmonary symptoms such as cough.[22] Thus, while some consider thickened feedings to be a basic element of conservative therapy in GER, it may not be beneficial in GER-associated pulmonary disease.

Total volume of feeding has been shown to be related to the duration of GER in infants with and without significant GER.[23] In this study, a feeding volume of 18 cc/kg resulted in almost twice as much GER as a feeding of 9 cc/kg. Several of the study infants who were allowed to take feedings ad libitum drank more than 30 cc/kg and had a proportional increase in the total duration of GER.[23] Thus, feeding volume is a significant determinant of GER for the first hour after a meal. It follows that limiting the volume of the feeding and positioning the infant immediately following the feeding may help to alleviate the symptoms of GER. However, if the volume of feedings is limited, it is necessary to ensure that an adequate volume of formula is taken over the course of 24 hours to meet metabolic needs and sustain adequate growth. Thus, in this setting, an increased frequency of feedings may be necessary.

When the possibility of GER in an infant with obstructive pulmonary disease is being considered, the absence of a secondary cause for GER should be established. In the simplest cases, a barium swallow and small bowel follow through will eliminate the possibility of anatomic obstruction of the upper gastrointestinal tract as an etiology for GER. The barium study is not a sensitive diagnostic evaluation for reflux, and so a negative study does not eliminate the possibility of GER. In addition, infants with cystic fibrosis have been treated for GER before the diagnosis of CF was made.[24-25] Therefore, sweat chloride concentration should be measured in infants with obstructive pulmonary disease in whom the diagnosis of GER is being considered. When these studies are unfruitful and the infant does not respond to simple conservative therapy for GER, then consultation with a pediatric gastroenterologist or pulmonologist may be warranted.

Summary

Gastroesophageal reflux should be considered in the evaluation of the infant with obstructive lung disease. Qualitative evidence of GER includes a history of regurgitation and nighttime pulmonary symptoms. Secondary causes of GER such as gastrointestinal obstruction should be eliminated by simple screening tests. Conservative measures that decrease gastric volume and avoid conditions that promote GER will be sufficient to eliminate the pulmonary symptoms in some infants. If wheezing persists, additional diagnostic evaluation should be initiated.

References

1. Herbst JJ. Gastroesophageal reflux. In: Lebenthal E, ed. *Textbook of Gastroenterology and Nutrition in Infancy.* 2nd Ed. New York, NY: Raven Press Ltd; 1989:803-813.
2. Meyers WF, Roberts DG, Herbst JJ. Value of tests for evaluation of gastroesophageal reflux in children. *J Pediatr Surg.* 1985:20:515-520.
3. Orenstein SR, Orenstein DM. Gastroesophageal reflux and respiratory disease in children. *J Pediatr.* 1988:112:847-858.
4. Christie DL. Respiratory disease associated with gastroesophageal reflux. *Pediatr.* 1979:63:344-345.
5. Pinkerton H. Oil and fats, their entrance into and fate in the lungs of infants and children: a clinical and pathologic report. *Am J Dis Child.* 1932:33:259-285.
6. Wolfson BJ, Allen JL, Panitch HB, Karmazin N. Lipid aspiration pneumonia due to gastroesophageal reflux: a complication of nasogastric feeding. *Pediatr Radiology.* 1989:19:545-547.
7. Mansfield LE, Stein MR. Gasteoesophageal reflux and asthma: a possible reflex mechanism. *Ann Allergy.* 1978:41:224-226.
8. Mansfield LE, Hameister HH, Spaulding HS, Smith NJ, Glab N. The role of the vagus nerve in airway narrowing caused by intraesophageal hydrochloric acid provocation and esophageal distention. *Ann Allergy.* 1981:47:431-434.
9. Spaulding HS, Mansfield LE, Stein MR, Sellner JC, Gremillion DE. Further investigation of the association between gastroesophageal reflux and bronchoconstriction. *J Allergy Clin Immunol.* 1982:69:516-521.
10. Neuhauser EBD, Berenberg W. Cardio-esophageal relaxation as a cause of vomiting in infants. *Radiology.* 1947:48:480-483.
11. Davies W. Cardio-chalasia in infancy. *J Pediatr.* 1952:41:467-472.
12. Hill El. Chair for infants with gastroesophageal incompetence. *Lancet.* 1953:2:71-72.
13. Rosenzweig JL. Cardio-esophageal relaxation. Treatment with an inexpensive chair. *J Pediatr.* 1954:44:574-577.
14. Meyers WF, Herbst JJ. Effectiveness of positioning therapy for gastroesophageal reflux. *Pediatr.* 1982:69:768-772.
15. Orenstein SR, Whittington PF, Orenstein DM. The infant seat as treatment for gastroesophageal reflux. *N Engl J Med.* 1983:309:760-763.
16. Orenstein SR, Whittington PF. Positioning for prevention of gastroesophageal reflux. *J Pediatr.* 1984:103:534-537.
17. Orenstein SR. Prone positioning in infant gastroesophageal reflux: Is elevation of the head worth the trouble? *J Pediatr.* 1990:117:184-187.
18. Minami H, McCallum RW. The physiology and pathophysiology of gastric emptying in humans. *Gastroenterology.* 1984:86:1592-1610.
19. Carre IJ. Postural treatment of children with a partial thoracic stomach (Hiatus hernia). *Arch Dis Child.* 1960:35:569-580.
20. Orenstein SR, Magill L, Brooks P. Thickening of infant feedings for therapy of gastroesophageal reflux. *J Pediatr.* 1987:110:181-186.
21. Bailey DJ, Andres JM, Danek GD, Pineiro-Carrero VM. Lack of efficacy of thickened feeding as treatment for gastroesophageal reflux. *J Pediatr.* 1987:110:187-189.
22. Orenstein SR, Salaby TM, Putman PE. Thickened feedings as a cause of increased coughing when used as therapy for gastroesophageal reflux in infants. *J Pediatr.* 1992;121:913-915.
23. Sutphen JL, Dillard VL. Effect of feeding volume on early postcibal gastroesophageal reflux in infants. *J Pediatr Gastroenterol Nutr.* 1988:7:185-188.
24. Frates JC, Cox KL. Cystic fibrosis mistaken for gastroesophageal reflux with aspiration. *Am J Dis Child.* 1981:135:719-720.
25. Thomas D, Rothberg RM, Lester LA. Cystic fibrosis and gastroesophageal reflux. *Am J Dis Child.* 1985:139:66-67.